



1031-00

A

PATENT

Attorney Docket No. ENDONET.023CP3

Date: October 30, 2000

Page 1

JC916 U.S. PTO
09/09/2002

10/30/00

ASSISTANT COMMISSIONER FOR PATENTS

WASHINGTON, D.C. 20231

ATTENTION: BOX PATENT APPLICATION

Sir:

Transmitted herewith for filing is the patent application of

Inventor(s):

For: METHOD AND DEVICE FOR TREATING GASTROESOPHAGEAL REFLUX DISEASE

Enclosed are:

(X) Twelve (12) sheets of drawing.

(X) Return prepaid postcard.

CLAIMS AS FILED

FOR	NUMBER FILED	NUMBER EXTRA	RATE	FEE
Basic Fee			\$355	\$355
Total Claims	37 - 20 =	17 ×	\$9	\$153
Independent Claims	4 - 3 =	1 ×	\$40	\$40
If application contains any multiple dependent claims(s), then add			\$270	\$N/A

**FILING FEE TO BE PAID
AT A LATER DATE**

(X) Please use Customer No. 20,995 for the correspondence address.

Gerard von Hoffmann
Registration No. 33,043
Attorney of RecordH:\DOCS\GVH\GVH-2753.DOC;jk/jt1
103000

INTELLECTUAL PROPERTY LAW

KNOBBE, MARTENS, OLSON & BEAR

A LIMITED LIABILITY PARTNERSHIP INCLUDING
PROFESSIONAL CORPORATIONS

PATENT, TRADEMARK AND COPYRIGHT CAUSES

620 NEWPORT CENTER DRIVE

SIXTEENTH FLOOR

NEWPORT BEACH, CALIFORNIA 92660-8016

(949) 760-0404

FAX (949) 760-9502

INTERNET WWW.KMOB.COM

LOUIS J. KNOBBE*
 DON W. MARTENS*
 GORDON H. OLSON*
 JAMES B. BEAR
 DARRELL L. OLSON*
 WILLIAM B. BUNKER
 WILLIAM H. NIEMAN
 ARTHUR S. ROSE
 JAMES F. LESNIAK
 NED A. ISRAELSEN
 DREW S. HAMILTON
 JERRY T. SEWELL
 JOHN B. SGANGA, JR.
 EDWARD A. SCHLATTER
 GERARD VON HOFFMANN
 JOSEPH R. RE
 CATHERINE J. HOLLAND
 JOHN M. CARSON
 KAREN VOGEL WEIL
 ANDREW H. SIMPSON
 JEFFREY L. VAN HOOSIER
 DANIEL E. ALTMAN
 MARGUERITE L. GUNN
 STEPHEN C. JENSEN
 VITO A. CANUSO III
 WILLIAM H. SHREVE
 LYNDIA J. ZADRA-SYMES*
 STEVEN J. NATUAUPSKY
 PAUL A. STEWART
 JOSEPH F. JENNINGS
 CRAIG S. SUMMERS
 ANNEMARIE KAISER
 BRENTON R. BABCOCK

THOMAS F. SMEGAL, JR
 MICHAEL H. TRENBOLM
 DIANE M. REED
 JONATHAN A. BARNEY
 RONALD J. SCHOENBAUM
 JOHN R. KING
 FREDERICK S. BERRETTA
 NANCY WAYS VENSKO
 JOHN P. GIEZENTANNER
 ADEEL S. AKHTAR
 GINGER R. DREGER
 THOMAS R. ARNO
 DAVID N. WEISS
 DANIEL HART, PH.D
 DOUGLAS G. MUEHLHAUSER
 LORI LEE YAMATO
 MICHAEL K. FRIEDLAND
 STEPHEN M. LOBBIN
 STACEY R. HALPERN
 DALE C. HUNT, PH.D
 LEE W. HENDERSON, PH.D
 DEBORAH S. SHEPHERD
 RICHARD E. CAMPBELL
 MARK M. ABUMERI
 JON W. GURKA
 ERIC M. NELSON
 MARK R. BENEDICT, PH.D
 PAUL N. CONOVER
 ROBERT J. ROBY
 SABING H. LEE
 KAROLINE A. DELANEY
 JOHN W. HOLCOMB
 JAMES J. MULLEN, III, PH.D

JOSEPH S. CIANFRANI
 JOSEPH M. REISMAN, PH.D
 WILLIAM R. ZIMMERMAN
 GLEN L. NUTTALL
 ERIC S. FURMAN, PH.D
 TIRZAH ABE LOWE
 GEOFFREY Y. IIDA
 ALEXANDER S. FRANCO
 SANJIVPAL S. GILL
 SUSAN M. MOSS
 JAMES W. HILL, M.D.
 ROSE M. THIESSEN, PH.D
 MICHAEL L. FULLER
 MICHAEL A. GUILIANA
 MARK J. KERTZ
 RABINDER N. NARULA
 BRUCE S. ITCHKAWITZ, PH.D
 PETER M. MIDGLEY
 THOMAS S. MCCLENANAHAN
 MICHAEL S. OKAMOTO
 JOHN M. GROVER
 MALLARY K. DE MERLIER
 IRFAN A. LATEEF
 AMY C. CHRISTENSEN
 SHARON S. NG
 MARK J. GALLAGHER, PH.D
 DAVID G. JANKOWSKI, PH.D
 BRAN C. HORNE
 PAYSON J. LEMEILLEUR
 DIANA W. PRINCE
 SHEILA N. SWAROOP

RAIMOND J. SALENIKS**
 DANIEL E. JOHNSON, PH.D.**
 JEFFERY KOEPKE, PH.D.**
 KHURRAM RAHMAN, PH.D
 JENNIFER A. HAYNES, PH.D
 BRENDAN P. O'NEILL, PH.D
 THOMAS Y. NAGATA
 YASHWANT VAISHNAV, PH.D
 MEGUMI TANAKA
 CHE S. CHERESKIN, PH.D.**
 ERIK W. ARCHBOULD
 PHILIP C. HARTSTEIN
 JULIE A. HOPPER
 CHRIS S. CASTLE
 JAMES W. AUSLEY
 R. P. CARDON, PH.D
 JENNIFER HAYES
 KIRK E. PASTORIAN, PH.D
 CHARLES T. RIDGELY
 KEITH R. MCCOLLUM
 BONNY YEUNG, PH.D
 CONNIE C. TONG, PH.D

* A PROFESSIONAL CORPORATION
 ** ALSO BARRISTER AT LAW (U.K.)
 ** U.S. PATENT AGENT

Assistant Commissioner for Patents
 Washington, D.C. 20231

DRAFTED BY JUSTIN R. STOTTS

CERTIFICATE OF MAILING BY "EXPRESS MAIL"

Attorney Docket No. : ENDONET.023CP3

Applicant(s) :

For : METHOD AND DEVICE FOR TREATING
GASTROESOPHAGEAL REFLUX DISEASE

Attorney : Gerard von Hoffmann

"Express Mail"

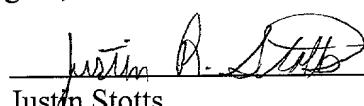
Mailing Label No. : EL559447741US

Date of Deposit : October 30, 2000

I hereby certify that the accompanying

Transmittal; Specification in 33 pages; 12 sheets of drawings; and Return Prepaid
Postcard

are being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and are addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.



 Justin R. Stotts

H:\DOCS\GVH\GVH-2754.DOC jk/103000

**METHOD AND DEVICE FOR TREATING GASTROESOPHAGEAL
REFLUX DISEASE**

The present application is a continuation-in-part of pending application Serial
5 No. 09/524,478 filed on March 13, 2000 which is a continuation-in-part of pending
application Serial No. 09/287,607 filed on April 7, 1999, entitled Submucosal
15 Esophageal Bulking Device, now U.S. Patent No. 6,098,629.

FIELD OF THE INVENTION

The present invention relates generally to the field of esophageal prosthetics.
10 More specifically, a prosthesis delivery device is disclosed for submucosal insertion of a
prosthetic bulking device.

BACKGROUND OF THE INVENTION

Gastroesophageal reflux is a physical condition in which stomach acids reflux,
or flow back from the stomach into the esophagus. Frequent reflux episodes (two or
15 more times per week), may result in a more severe problem known as gastroesophageal
reflux disease (GERD). Gastroesophageal reflux disease is the most common form of
dyspepsia, being present in approximately 40% of adults in the United States on an
intermittent basis and some 10% on a daily basis.

Dyspepsia, or heartburn, is defined as a burning sensation or discomfort behind
20 the breastbone or sternum and is the most common symptom of GERD. Other
symptoms of GERD include dysphasia, odynophagia, hemorrhage, water brash, and
pulmonary manifestations such as asthma, coughing or intermittent wheezing due to
acid aspiration. Dyspepsia may also mimic the symptoms of a myocardial infarction or
severe angina pectoris. Many factors are believed to contribute to the onset of GERD
25 including transient lower esophageal sphincter relaxations, decreased LES resting tone,
delayed stomach emptying, and an ineffective esophageal clearance. Many in the field
agree, however, that the primary cause of GERD is the lack of competency of the lower
esophageal sphincter.

The lower esophageal sphincter, or valve, is comprised of smooth muscle
30 located at the gastroesophageal (GE) junction and functions to allow food and liquid to
pass into the stomach but prevent regurgitation of stomach contents. At rest, the LES

maintains a high-pressure zone between 10 and 30 mm Hg above intragastric pressure. Upon deglutition, the LES relaxes before the esophagus contracts, allowing food to pass through into the stomach. After food passes into the stomach, the LES contracts to prevent the stomach contents and acids from regurgitating into the esophagus. The mechanism of LES opening and closing is influenced by innervation via the vagus nerve and hormonal control of gastrin and possibly other gastrointestinal hormones.

The severity of GERD varies from patient to patient and in extreme cases complications including esophageal erosion, esophageal ulcers, and esophageal stricture are observed. Esophageal stricture is a serious condition which results from prolonged exposure of the esophageal mucosa to acid reflux. The most common clinical manifestation of stricture is dysphasia. Unlike dysphasia from non-strictured esophageal reflux, dysphasia caused by stricture is progressive in that the size of a bolus which can pass into the stomach progressively becomes smaller. In addition to esophageal erosion and ulceration, prolonged exposure of the esophageal mucosa to stomach acid can lead to a condition known as Barrett's Esophagus. Barrett's Esophagus is an esophageal disorder that is characterized by the replacement of normal squamous epithelium with abnormal columner epithelium. This change in tissue structure is clinically important not only as an indication of severe reflux, but the appearance of columner epithelium in the esophagus is indicative of cancer.

Current methods to treat gastroesophageal reflux disease consist of lifestyle changes such as weight loss, avoidance of certain foods that exacerbate the symptoms of GERD and avoidance of excessive bending. Elevation of the head of the bed helps prevent nocturnal reflux. While these avoidance strategies may be helpful, there is relatively little data supporting the efficacy of lifestyle modification alone for the treatment of GERD.

Medications for the treatment of GERD have been administered for years with little or no success. Conventional antacids, such as TUMS® and ROLAIDS®, produce short-term relief, but often have side effects including diarrhea and constipation. H₂ receptor antagonists, such as Cimetidine and Ranitidine, are relatively more effective in controlling GERD symptoms but these symptomatic therapies fail to treat the underlying cause of the disease. More powerful secretory inhibitors, such as the proton

pump inhibitors Omeprazole and Lansoprazole are more effective than the H2 antagonists but these drugs are expensive and, in the long term, produce negative side effects.

Surgery has become an attractive alternative for the treatment of GERD when
5 lifestyle modification and medications fail to treat this debilitating condition. There are numerous reflux operations available which perhaps reflect the inadequacy of any one procedure to totally control the problem. The most commonly performed operation, Nissen Fundoplication, has been effective, but is often complicated by stricture formation or gas bloat syndrome. A laparoscopic Nissen procedure has also been
10 developed, adding another dimension of difficulty, and long-term results remain questionable. In addition, a percutaneous laparoscopic technique has been developed.
(See, for example, U.S. Patent No. 5,006,106 to Angelchik). Minimally invasive techniques, such as transesophageal implantation of a prosthetic valve have also been attempted. (See, for example, U.S. Patent No. 4,846,836 to Reich). Despite extensive
15 attempts in the field to treat and prevent GERD, existing forms of treatment all have shortcomings.

In view of the foregoing, and notwithstanding the various efforts exemplified in the prior art, there remains a need for a minimally invasive bulking prosthesis and deployment methodology for transesophageal delivery into the vicinity of the lower esophageal sphincter.
20

SUMMARY OF THE INVENTION

There is provided in accordance with one aspect of the present invention, a method of implanting a bulking device beneath the mucosa in the lower esophagus. The method comprises the steps of puncturing the mucosa with a device having a first cross-sectional area, and creating a pocket beneath the mucosa in communication with the puncture. The puncture is enlarged, and a bulking device is introduced through the puncture and into the pocket.
25

Preferably, the introducing step comprises introducing an expandable bulking device. The bulking device is expandable from an introduction cross-sectional area to an enlarged cross-sectional area, and the introduction cross-sectional area is greater than
30

the first cross-sectional area. Preferably, the introducing step comprises introducing a hydrogel bulking device.

In one embodiment, the creating a pocket step comprises introducing a volume of fluid beneath the mucosa. The volume of fluid is generally within the range of from 5 about 0.5 cc to about 5 cc.

The enlarging step comprises introducing a dilator through the puncture. In one embodiment the dilator removably carries an introducer sheath. The dilator is removed from the introducer sheath, and the bulking device is thereafter introduced through the introducer sheath and into the pocket.

10 In accordance with another aspect of the present invention, there is provided a method of treating a condition in the lower esophagus. The method comprises the steps of creating a pocket beneath the mucosa in the lower esophagus, and positioning an expandable bulking device within the pocket. Preferably, the expandable bulking device comprises a hydrogel. The bulking device has a cross-section prior to implantation within the range of from about 0.2 mm to about 5 mm. In certain embodiments, the bulking device has a cross-section prior to implantation of no more 15 than about 3 mm, or no more than about 2 mm.

The method may further comprise the step of explanting the bulking device from the pocket. The explanting step may be accomplished using suction.

20 In accordance with a further aspect of the present invention, there is provided a method of explanting a bulking device positioned beneath the mucosa in the vicinity of the lower esophageal sphincter. The method comprises the steps of locating a bulking device positioned beneath the esophageal mucosa, and establishing a passage through the mucosa. The bulking device is explanted through the passage. The passage may be 25 formed by suction, or by the use of a cutting tool such as a sharpened instrument, RF electrode or laser.

30 In accordance with a further aspect of the present invention, there is provided a method of implanting a bulking device beneath the mucosa in the lower esophagus. The method comprises the steps of puncturing the mucosa with a device having a first cross-sectional area, and enlarging the puncture. The expandable bulking device is thereafter

introduced through the puncture to a position beneath the mucosa. The enlarging step preferably comprises advancing a dilator through the puncture.

Further features and advantages of the present invention will become apparent to those of skill in the art in view of the detailed description of preferred embodiments which follows, when considered together with the attached drawings and claims.

BRIEF DESCRIPTION OF THE DRAWINGS

FIGURE 1 is a schematic view of a pair of gastroesophageal bulking prostheses in accordance with the present invention, positioned at about the junction between the esophagus and the stomach, before expansion, in which the LES is in an open configuration.

FIGURE 2 is a schematic view as in Figure 1, following expansion of the prostheses, in which the LES is illustrated in a closed configuration.

FIGURE 3 is a perspective schematic view of an esophageal bulking device of the present invention.

FIGURE 4 is a perspective schematic view of another esophageal bulking device of the present invention.

FIGURE 5 Is a cross-sectional perspective view of an esophageal bulking device of the present invention.

FIGURE 6 illustrates an embodiment of an esophageal bulking device of the present invention having surface regions which promote tissue ingrowth.

FIGURE 7 is a fragmentary perspective view of an endoscope positioned within the esophagus prior to formation of a blister or pocket for receiving a bulking device.

FIGURE 8 is a schematic cross-sectional view of the endoscope positioned within the esophagus, forming a pocket by fluid injection.

FIGURE 9 is a side elevational view as in FIGURE 8, illustrating an access incision.

FIGURE 10 is a side elevational view as in FIGURE 9, illustrating a mechanical dilatation catheter during insertion into the blister.

FIGURE 11 is a side elevational view as in FIGURE 10, with the mechanical dilatation catheter enlarged within the blister.

FIGURE 12 is a side elevational view as in FIGURE 11, illustrating the cavity formed by the dilatation catheter.

FIGURE 13 is a top view of a blister, prior to forming a pocket with a cutting tool.

5 FIGURE 14 is a top view as in FIGURE 13, with the cutting tool inserted within the blister.

FIGURE 15 is a top view of the blister as in FIGURE 14, with the cutting tool cutting a pocket in the fibrous submucosa layer.

10 FIGURE 16 is a side elevational cross-section through a cap for attachment to an endoscope to deliver a submucosal prosthesis.

FIGURE 17 is a side elevational schematic view of an overtube in accordance with the present invention, for receiving an endoscope to deliver a submucosal prosthesis.

15 FIGURE 17A is a bottom view of the overtube illustrated in FIGURE 17.

FIGURE 18 is a side elevational schematic view of a bulking device deployment catheter, such as for "blind" deployment.

FIGURE 19 is a side elevational schematic view of a prosthesis delivery needle assembly.

20 FIGURE 20 is an enlarged cross-sectional view of the distal end of the delivery needle of FIGURE 19.

FIGURE 21 is a side elevational view of the distal end shown in FIGURE 20, with the plunger distended to eject a bulking element.

FIGURE 22 is a side elevational view of an alternate distal end of a deployment catheter, adapted to deploy an inflatable balloon.

25 FIGURE 23 is an exploded, schematic view of an overall reflux repair system in accordance with the present invention.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

Referring to FIGURE 1, there is illustrated a schematic representation of the stomach 10 and a portion of the lower esophagus 12. The esophagus 12 extends through the diaphragm 14, below which the esophagus 12 communicates with the interior of the stomach 10. A pair of gastroesophageal prosthetic bulking devices 16, in

accordance with the present invention, is illustrated at about the junction between the lower esophagus 12 and the stomach 10.

In the illustrated embodiment, the bulking device 16 is delivered in the submucosa 17. The submucosa 17 is a fibrous layer of tissue positioned between the mucosa 15 and a layer of circular muscle 19. The circular muscle 19 is surrounded by a layer of longitudinal muscle 21, as is well understood in the art. The bulking device 16 may be delivered in the mucosa or beneath the mucosa 15 as is discussed elsewhere herein. In particular, the bulking device 16 may be delivered within the submucosa 17 as illustrated, or at the interface of adjacent tissue planes, such as between the mucosa 15 and submucosa 17, beneath the muscularis mucosa or between the submucosa 17 and circular muscle 19. Preferably, the bulking device 16 is positioned radially inwardly from the circular muscle layer 19.

Although the anatomy illustrated in FIGURE 1 is generally normal, except for the improperly functioning native lower esophageal sphincter, the present invention is also useful in patients having lower esophageal abnormalities, such as hiatal hernia. In this condition, a portion of the wall of the stomach 10 extends upwardly through the diaphragm 14 and herniates superiorly to the diaphragm 14. The existence of a hiatal hernia or another abnormality in the lower esophagus may affect the delivered position of the esophageal prosthetic bulking device 16, but may not disqualify a patient otherwise treatable with the prosthetic bulking device 16 of the present invention.

As illustrated in FIGURE 1, the esophageal bulking device 16 is generally delivered below the mucosa such as in the submucosa or between adjacent tissue planes in the vicinity of the sphincter. The submucosa is a springy, fibrous tissue, which needs to be expanded in order to produce a cavity for delivery of the bulking device 16. Alternatively, the submucosa can be cut using mechanical cutting techniques or cautery tools as is discussed in more detail below.

Ideally, the esophageal bulking device 16 is delivered in a position that extends across or is closely adjacent to the sphincter so that residual sphincter activity is optimized and the mucosal regions of the esophagus are protected from acid reflux. The precise positioning of the prosthesis 16 depends largely on the patient's anatomy and the severity of GERD, and will be a matter of clinical choice at the time of delivery. In

patients with a hiatal hernia, for example, the esophageal bulking device 16 is delivered as close as possible to the sphincter but care must be taken to insure that the hernia will not perturb the operation of the bulking device 16.

Advantageously, the esophageal bulking device 16 of the present invention
5 enhances any residual closing pressure function and length of the sphincter so as to effectively reduce or prevent the reflux of stomach contents into the esophagus. In an open or relaxed state, as shown in FIGURE 1, the esophageal bulking device allows food and liquid to pass through the esophagus into the stomach. However, when the sphincter is closed, as shown in FIGURE 2, the esophageal bulking device increases the
10 closing pressure along a sufficient axial length that, in cooperation with the contraction of the sphincter, it inhibits or prevents the reflux of stomach contents.

Depending on the degree of LES dysfunction, more than one esophageal bulking device 16 can be delivered into the lining of the esophagus. With the 4 mm to 6 mm expanded diameter hydrogel bulking device discussed below, for example, anywhere
15 from one to about six or more bulking devices may be implanted based upon a particular patient's condition. Where two or three or more esophageal bulking devices 16 are utilized to improve LES function, the bulking devices 16 may be spaced around the circumference of the LES. Generally, multiple bulking devices 16 will be located substantially in the same transverse plane perpendicular to the longitudinal axis of the
20 esophagus. Use of multiple bulking devices 16 without rigid interconnection permits the LES to radially expand to a greater degree so as to permit bolus passage and better accommodate the natural function of the esophagus.

Depending on the patient's anatomy and the extent of GERD, esophageal bulking devices 16 having various lengths and cross sectional profiles are delivered so as to maximize operation with the residual LES function. Using common esophageal manometry and endoscopic techniques, for example, medical personnel can measure the degree of closure (e.g., closing pressure) achieved by the sphincter as well as any unique anatomical features of the lower esophagus for a particular patient when selecting specific shapes and designs of esophageal bulking devices 16 to be delivered.
25

Due to the irregular cross-sectional configuration of the closed sphincter, the cross-sectional configuration of the bulking device 16 can take on any of a wide variety
30

of shapes including, but not limited to, those specific embodiments disclosed herein. In general, the desired expanded transverse plane thickness of the esophageal bulking device 16 will depend on the lumen diameter and the extent of LES dysfunction. Devices 16 produced in accordance with the present invention can be rated according to their bulking area, which represents the total cross-sectional area the device will occupy within the region at or about to the sphincter, referred to as the “bulking zone”. In general, a larger transverse cross-sectional area will produce a higher closing pressure for a given state of the disease.

FIGURES 3, 4, 5 and 6 illustrate different configurations and features of certain esophageal bulking device embodiments of the present invention. The esophageal bulking device 16 generally comprises an oblong, cylindrical, elliptical, toric or pillow shape and has a proximal end 18 and a distal end 20. As used herein, “distal” shall refer to a location closer to the stomach and “proximal” shall refer to a location closer to the mouth. In one embodiment, a proximal portion 23 has a smaller cross-sectional area than a distal portion 25. Alternatively, embodiments of the esophageal bulking device 16 can be a cylindrical shape (FIGS. 4, 6 and 19-22) or elliptical shape (not illustrated) wherein a proximal portion 23 and a distal portion 25 have roughly the same cross-sectional area and shape. The bulking device 16 preferably substantially retains its pre-implanted configuration once delivered into the body.

Suitable esophageal bulking devices 16 comprise a soft, flexible body that may have an expanded axial length from 0.5 cm to 5.0 cm, a width (circumferential direction) of 0.2 cm to 2.0 cm, and a thickness (radial direction) of 0.2 cm to 2.0 cm. Many esophageal bulking devices 16 of the present invention have a length within the range of 1.0 cm to 4.0 cm, a width within the range of 0.2 cm to 1.5 cm, and a thickness within the range of 0.2 cm to 1.5 cm. In one embodiment, the esophageal bulking device 16 has a length of 2.0 cm to 3.0 cm, a width of 0.8 cm to 1.0 cm, and a thickness of 0.4 cm to 0.6 cm. The cross-sectional configuration may be circular, oval or other configuration, as desired.

Length to cross section or thickness ratios are generally no more than about 15:1 and are often no more than about 6:1 or 4:1. Length to thickness ratios on the order of less than 3:1 may also be desirable depending upon the severity of the condition. The

cross-sectional area of the bulking device 16 may also vary at different points along the length of the same device 16. As mentioned above, optimal dimensions may be patient specific and can be determined through routine experimentation of one of skill in the art in view of the disclosure herein.

5 An LES having a relaxed open diameter of 2.0 cm, for example, has a cross-sectional lumen area of 3.14 cm^2 . A 25% bulking function could be accomplished by providing a bulking device 16 having a total cross-sectional area in the bulking zone of about 0.785 cm^2 . The bulking area may represent the area of an esophageal bulking device 16 having a generally oval or rectangular cross-section (e.g., $0.443 \text{ cm} \times 1.772 \text{ cm}$) which is adapted to extend axially for a length of 1 to 3 cm beneath the mucosa.

10 In general, the objective of the present invention is to increase the closing pressure and length of the lower esophageal sphincter. The present inventors believe that a closing pressure of at least a certain minimum closing threshold value, maintained along a minimum axial effective LES length will satisfactorily reduce esophageal reflux. In the intra-abdominal (*i.e.*, inferior to the diaphragm 14) esophagus, about 2 cm 15 of effective LES length appears desirable. An average pressure along that length is preferably in excess of about 10 mm Hg, preferably at least about 15 mm Hg, and optimally in the range of from about 15 mm to about 30 mm Hg.

20 Within certain outer limits, any increase in the closing pressure in the LES may improve symptoms. For example, some patients have an LES closing pressure on the order of about 5 mm Hg, which is accompanied by severe GERD symptoms. At the high end, a closing pressure in excess of about the minimum diastolic pressure inhibits blood flow, thereby increasing the risk of localized pressure necrosis. Pressure slightly below the minimal diastolic pressure may still interfere with swallowing function. The 25 present invention therefore preferably enables increasing the closure pressure from a pretreatment value below about 10 to 15 mm Hg to a post treatment value of preferably on the order of from about 18 or 20 to about 25 or 30, along a length of at least about 1.0 cm and preferably at least about 2 cm or 2.5 cm or more.

Once the total desired cross-sectional area and length of the bulking device is 30 determined for a particular patient or class of patients, the allocation of that cross-sectional area to a single bulking device or a series of bulking devices which together

produce the desired cross-sectional area must be determined. This clinical decision will take into account any unique aspects to the patient's lower esophageal anatomy, together with the extent of the disease and consequent total area of bulking required. In general, a larger single bulking device will require a larger submucosal pocket for delivery and the consequent greater disruption of tissue in the immediate area of the prosthesis, which may be undesirable in some patients. In addition, a larger single device may have a greater likelihood of migration which would be reduced if the same total prosthesis volume was delivered in two bulking devices each having half the cross-sectional area of the single larger device.

The bulking device 16 is preferably flexible and has a high degree of softness which approaches that of the native mucosal tissue, to minimize trauma to the adjacent tissue. The material of the bulking device 16 is thus preferably soft enough so that it is incapable of exerting sufficient localized pressure to cause pressure necrosis. A localized pressure in excess of about 70 mm Hg gives rise to a risk of localized tissue necrosis. As will be understood by those of skill in the art, the configuration of the bulking device 16 (e.g. sharp edges, etc.) operates in cooperation with the softness of the construction materials to optimize the compatibility of the bulking device. A smooth, bluntatraumatic outer surface is preferred.

One suitable bulking device construction comprises the use of an inflatable pillow or balloon, partially or completely filled with a liquid or semi-liquid, which allows one end to be compressed by peristaltic compression and the other end to expand bulbously. The ability of the volume of the bulking device to flow from one end of the bulking device to the other and back permits the passage of a peristaltic wave, as will be appreciated by those of skill in the art in view of the disclosure herein. Suitable elastomeric balloons comprise material such as silicone, latex, urethane, and others as will be understood by those of skill in the art.

In addition to being soft, the bulking device in some embodiments may also be compressible. This enables the filler 24 and body of bulking device 16 to expand when nothing is passing through the LES, but compress, for example, to no more than about 4 mm and preferably no more than about 2 mm in radial thickness during swallowing. After swallowing, the filling material 24 and body will desirably rebound back to

PCT/US2014/042099

facilitate the LES closure function. In this manner, the bulking device 16 can cooperate with any residual function of the LES to minimize the occurrence of reflux.

Referring to FIGURE 5, the bulking device 16 generally comprises an outer surface 26 which encloses a filler 24 therein. The outer surface 26 may be homogeneous with the filler 24, or may be the surface of a dissimilar material in the form of a flexible wall 27 to encapsulate the filler. A homogeneous material outer wall 27 may be provided with a different physical property than the filler 24, such as by heat treatment, solvent exposure or the like to provide a barrier coating around the filler 24.

The esophageal bulking device 16 can be manufactured as a unitary or multi-component structure in a variety of ways as will be appreciated by those of skill in the art in view of the disclosure herein. The bulking device 16, for example, may be a unitary structure molded or formed as a single piece of biocompatible foam material such as silicone foam or polyurethane foam, or may be cut from a block of such foam. Such foam parts can be made with an outer skin 26 of porous foam that facilitates tissue ingrowth. Hydrogel bulking devices are disclosed in detail below.

Alternatively, the esophageal bulking device 16 can comprise a body having at least two components connected together and can be made, for example, by positioning an outer sleeve or layer 27 of porous material such as expanded polytetrafluoroethylene (PTFE) or other tissue ingrowth material around the filler 24 by either a simple filling operation or by bonding the two materials together. If expanded PTFE is used, a PTFE surface etching step prior to bonding with a silicone based glue may be performed. Alternatively, a process of gluing by simultaneously compressing and heating a stack-up of foam, glue and PTFE can be employed. The outer layer 27 may be secured to the bulking device 16 in any of a variety of manners, such as by solvent bonding, thermal bonding, adhesives, and others as will be apparent to those of skill in the art in view of the disclosure herein.

The present inventors further contemplate embodiments of the esophageal bulking device 16 which have surface textures, coatings or structures to resist migration. In general, the entire outer surface 26 of the outer layer 27 or filler 24 can be coated or textured to facilitate tissue attachment such as by cellular ingrowth. The resulting attachment surface 26 can be integral with the bulking device 16 or can be directly or

indirectly connected to the bulking device 16 so that the device 16 can be positioned and retained in the desired position within the esophageal wall. The outer surface 26 may additionally, or alternatively, be provided with any of a variety of tissue retention structures such as hooks, barbs, tacks, clips, sutures, staples, tissue adhesives, attachment strips, attachment spots, attachment connectors, or other attachment means which will be understood by those of skill in the art in view of the disclosure herein.

As illustrated in FIGURE 6, one embodiment of the present invention is alternatively provided with one or more attachment surfaces 28 spaced about the device 16 so as to facilitate tissue ingrowth from the adjacent tissue over less than the entire surface 26 of the implant. The design, spacing and total surface area of the attachment surfaces 28 can be varied widely, depending upon the clinical objective.

For example, in an embodiment in which removal is not anticipated, the tissue ingrowth surface area can be as high as 75% to 100% of the surface 26 of the bulking device 16. Alternatively, in an application where the bulking device 16 is preferably removable after a period of time, the percentage of cellular ingrowth surface is preferably kept to the minimum required to reasonably resist migration within the esophageal wall. Thus, in some embodiments, the tissue ingrowth surface 28 covers no more than about 20% and possibly no more than about 5% of the total surface area of the bulking device 16. In this manner, trauma to the tissue upon removal of the bulking device 16 can be minimized. The ease of removal of the bulking device 16 may be desirable because new implants which better accommodate the changing anatomy of the patient during the progression of the patient's LES dysfunction and/or age may be indicated.

In one embodiment, one or more attachment zones 28 may extend circumferentially around the bulking device 16. Alternatively, the tissue ingrowth surfaces 28 may extend axially along the length of the esophageal bulking device 16. Further, the attachment zones 28 can be provided in the form of spots or patches distributed around the surface of the esophageal bulking device 16.

The porosity of the cellular ingrowth regions 28 may range from about 20 μm to about 100.0 μm or greater. Desirably, the porosity of the cellular ingrowth regions 28

ranges from 20 μm to 50 μm and, in many embodiments, the porosity of the cellular ingrowth regions 28 ranges from 20 μm to 30 μm .

Suitable outer layer 27 and/or attachment surface 28 materials include polytetrafluoroethylene (PTFE), polyethylene terephthalate, polyester, polyurethane, 5 silicone, Dacron, polypropylene knit, and other materials which will be apparent to those of skill in the art in view of the present disclosure. In one embodiment of the invention, the cellular ingrowth region 28 comprises PTFE having a 22 μm pore size. This porosity appears to permit shallow ingrowth into the esophageal bulking device 16 to prevent axial migration of the device 16 along tissue planes yet allows for relatively 10 easy explant.

Delivery of the esophageal bulking device 16 below the mucosa can be accomplished in any of a variety of ways, as will be apparent to those of skill in the art in view of the disclosure herein. Delivery systems can be specially constructed or assembled from existing endoscopic and other surgical tools to accomplish the basic 15 delivery steps.

In general, the delivery site for a particular patient is identified, such as by endoscopy and manometry. Tissue adjacent to the delivery site is preferably immobilized to permit a puncture or incision to be made. Immobilization of the esophageal lining may be accomplished by grasping the tissue utilizing forceps, such as 20 those which may be advanced through a working channel on an endoscope. Alternatively, a vacuum may be applied to a lumen through an endoscope to immobilize the tissue.

Using counter-traction on the tissue applied by way of the tissue grasper or 25 vacuum, the mucosa is pierced to enable insertion of the prosthesis. The mucosal layer may be pierced in a variety of ways, as will be recognized in the art. In accordance with one aspect of the present method, a needle is utilized to pierce the mucosa and create a blister by injecting a volume of fluid such as saline solution. Alternatively, an electrocautery cutter or any of a variety of sharp dissection tools may be utilized to pierce the mucosa and provide access to the submucosal area.

Once an aperture has been formed in the mucosa, a pouch or cavity is formed in 30 the submucosa. The pouch may be formed by liquid infusion to enlarge the blister

discussed above. Alternatively, any of a variety of blunt tools may be utilized to achieve a blunt dissection in the submucosa or between adjacent tissue planes to form a pouch for receiving the prosthesis. Alternatively, an inflation device, such as a balloon, may be specially shaped for insertion and inflation to separate submucosal tissue and provide a submucosal pouch.

5

10

15

20

25

30

Following formation of a submucosal pouch, one or more bulking devices 16 are introduced therein. The bulking device 16 may be inserted by way of a grasper, clamshell deployment device, or other tools. Depending upon the shape and compliancy of the bulking device 16, the bulking device 16 may be deployed from the distal end of a tubular element, such as by advancing an axially moveable core to push the prosthesis from the distal end of the tube. One or more pull elements such as wires, strings or tabs may be provided on the bulking device 16, so that a distally extending pull element may be advanced into the pouch under distal force using a grasper, or a second mucosal puncture inferior to the primary mucosal puncture may be provided through which to pull a pull element, thereby advancing the bulking device 16 inferiorly into the pouch.

Following placement of the bulking device 16 into the submucosal pouch, the mucosal opening closes naturally or can be closed using any of a variety of closure techniques. A conventional suture, ligating bands or staples or other clips, may be utilized endoscopically, as will be understood in the art. Alternatively, a topical glue or other adhesive patch may be utilized to close the opening in the mucosa.

Thus, referring to FIGURES 7 and 8, there is schematically illustrated one method of providing a blister or pocket below the mucosa. A portion of the esophagus 12 is illustrated, having a mucosa 15, submucosa 17 and circular muscle layer 19. An endoscope 30 is nasally or orally introduced and trans-esophageally advanced until a distal end 32 is positioned in the vicinity of the desired bulking device delivery site. A portion 34 of the mucosa 15 is raised into a blister, such as by introduction of a hypodermic needle 36 from the distal end 32 of endoscope 30. Hypodermic needle 36 is utilized to inject a fluid media 38 such as n-saline or other biologically acceptable material below the mucosa 15 to form a blister 40. Proper positioning of the hypodermic needle 36 can be ascertained by tactile feedback and

visualization through the endoscope as is understood in the art. Alternatively, the portion 34 of mucosa 15 can be raised from the submucosa 17, such as by application of a vacuum to the wall of the esophagus.

The cavity may be formed entirely by the injection of saline or other injectable media, or may be formed into its final size using mechanical tools as discussed below.

Following blister formation, a small incision or access site 42 is provided as illustrated in FIGURE 9. A cavity formation device, such as a balloon dilatation catheter 44, may be introduced through the access site 42 and into the blister. See figures 10-12. The balloon 46 is inflated, thereby forming a pocket 40 within the esophagus wall. If the bulking device 16 is to be delivered within the submucosa 17, the balloon dilatation catheter 44 must generally inflate to a larger volume than the volume of the bulking device 16, due to recoil of the fibrous tissue in the submucosa 17.

Following dilatation or manipulation of another pocket forming device, the balloon dilatation catheter 44 or other device is reduced in size and removed, thereby leaving a receiving cavity 46 for one or more bulking devices 16. The bulking device 16 may then be inserted within the cavity using any of a variety of delivery implements, the specific design of which will depend upon the size and configuration of the bulking device 16. Alternatively, the bulking device may be introduced into the cavity through a delivery lumen extending throughout the balloon catheter. The foregoing steps may be repeated for two or more positions around the circumference of the esophagus in the vicinity of the LES, as may be desired.

An alternate method of forming the cavity 46 is illustrated in FIGURES 13-15. In this embodiment, a mechanical cutting device, such as a scissor 48, is introduced below the mucosa 15 and manipulated to sever the springy tissue of the submucosa 12 and produce a cavity 46 for receiving the submucosal bulking device 16.

Referring to FIGURE 16, there is illustrated a distal end construction for a medical device which permits reproducible access to a delivery site below a tissue surface. Notwithstanding the utility of the previously described access and delivery methods, the reproducibility of each depends upon the technical skills of the clinician.

The devices illustrated in FIGURES 16-18 and 23 enhance procedure to procedure

PCT/US2002/022553

reproducibility of a submucosal prosthesis delivery, and minimize variability due to clinical experience and technical skill.

The distal end construction illustrated in FIGURE 16 is in the form of a cap which may be integrally manufactured with or subsequently attached to the distal end of an endoscope or other elongate medical device. The cap 50 comprises a sidewall 52 which is generally in the form of tubular element although other constructions may be utilized. Sidewall 52 may be made from any of a variety of biocompatible metals or polymers, such as polycarbonate, acrylic, HDPE, nylon, PTFE, stainless steel, and others well known in the medical device arts. In one embodiment, the cap 50 has an axial length of about 2.2 inches, an outside diameter of about 0.6 inches, and side wall thickness of about 0.06 inches.

The sidewall 52 extends between a proximal end 54 and a distal end 56. Distal end 56 preferably blunt, and may include a distally extending pliable nose or extension such as molded silicone, to provide an atraumatic surface. The cap 50 is provided with an opening 58, preferably on the side wall 52, for receiving tissue from the target site. In one embodiment, the opening 58 has an axial length of about 1.25 inches, and a width of about 0.28 inches. In this embodiment, a generally rectangular opening 58 is provided to facilitate introduction of an elongate bulking element into the target site. Other configurations for first opening 58 may be utilized, as is discussed below, depending upon the size and shape of the prosthesis.

A tissue stabilizing or limit surface 62 defines at least a portion of the wall of the cavity. In the illustrated embodiment, surface 62 is on the lateral face of a surface such as on a shelf or plate 60 positioned medially (towards the central longitudinal axis) from the first opening 58. Preferably, the tissue stabilizing surface 62 is provided with one or more apertures 64, which are in communication through the shelf 60 with a vacuum lumen 66 in the cap 50. Vacuum lumen 66 is adapted for coupling to a lumen in the endoscope or other medical device, so that a vacuum may be drawn on vacuum lumen 66.

The tissue stabilizing surface 62 cooperates with the tissue opening 58 to define a tissue receiving cavity 65 in the medical device. The overall shape and volume of the cavity 65 can be varied widely, depending upon the intended application. For example,

PCT/US2012/046268

tissue opening 58 can have a generally rectangular shape as in the illustrated embodiment. Alternatively, the tissue opening 58 can be in the form of an oval or ellipse, or circle, depending upon the length and width of the desired submucosal low pressure zone or prosthesis. In addition, the tissue stabilizing surface 62 can be concave in the direction of tissue opening 58 or generally planar as illustrated. In one embodiment, the tissue stabilizing surface 62 is in the form of a portion of the side wall of a cylinder, such that it has a substantially linear configuration in the axial direction and a radiused curve in the transverse cross-section. Generally conical or hemispherical configurations for tissue stabilizing surface 62 may also be provided, with an aperture 64 at the apex thereof or a plurality of apertures 64 positioned on the tissue stabilizing surface 62. The tissue stabilizing surface 62 may also be provided with friction enhancing structures, such as a plurality of ridges or grooves to minimize sliding of the submucosal tissue along the surface 62.

In use, tissue which is positioned adjacent the tissue opening 58 will be drawn into the tissue opening 58 and adjacent the tissue stabilizing surface 62 in response to application of vacuum through apertures such as the apertures 64. The tissue stabilizing surface 62 thus acts as a limit, to reproducibly control the amount of tissue drawn into the opening 58 in response to the vacuum.

The cap 50 may be provided at its proximal end 54 with a second opening 68. Second opening 68 is adapted to be coupled to an endoscope or other medical device. For this purpose, an attachment structure 70 such as an annular recess may be provided on the proximal end 54 to facilitate insertion of the distal end of an endoscope (not shown) therein. The cap 50 may be secured to the endoscope in any of a variety of ways, such as by threaded engagement, snap fit or other interference fit structures, adhesives, or other attachment techniques which will be known in the art.

When coupled to an endoscope, a viewing lens on the endoscope is preferably oriented in the cap 50 such that tissue which has advanced into the cavity 65 can be visualized through the endoscope optics. This may be accomplished by constructing the shelf 60 from a transparent material, and/or providing a viewing aperture 72 between the lens on the endoscope and the tissue opening 58.

A working channel on the endoscope is aligned with a deployment lumen 74. Deployment lumen 74 may be defined at least in part by an internal baffle wall 76. In the illustrated embodiment, the baffle 76 is inclined radially outwardly in the distal direction to taper the inside diameter of the deployment lumen 74 in the distal direction.

5 This assist in guiding the deployment device (discussed in greater detail below) and possibly the cavity forming device into the tissue which has been drawn into the cavity

10 65. The deployment lumen 74 has a distal end 78. Deployment lumen 74 is oriented such that an elongate device which is advanced through deployment lumen 74 and out distal end 78 will extend at least partway across the tissue opening 58. A piercing device such as a needle, cautery tip or other cutting structure which is advanced through deployment lumen 74 will enter and travel beneath tissue which is brought into contact with tissue stabilizing surface 62.

Referring to FIGURES 17 and 17A, there is illustrated a side elevational view of an overtube embodiment adapted to be advanced proximally over the distal end of an endoscope and pulled proximally like a sheath to adapt the endoscope for the present application. In an alternate application, discussed in connection with Figure 18, infra, the distal end configuration is on an access catheter without an associated endoscope.

In the illustrated embodiment, a flexible tubular sheath 80 extends proximally from the distal end assembly 56. Tubular sheath 80 is preferably dimensioned to receive and closely fit a standard endoscope. For example, one common endoscope for use in the present invention has an outside diameter of about 9.8 mm. The corresponding lumen 120 in tubular sheath 80 has an inside diameter of about 11 mm and an axial length within the range of from about 60 cm to about 120 cm. Tubular sheath 80 may comprise any of a variety of polymeric materials which are conventional in the catheter manufacturing arts. The tubular sheath 80 may be integrally formed with or bonded to the side wall 52 of midsection 53 and other structural components of the distal end 56 assembly. In one embodiment, tubular sheath 80 comprises PVC, having a wall thickness of about 0.050".

A proximally extending deployment lumen 74 is defined within a tubular wall 82. In this construction, the tubular wall 82 extends in parallel with at least a portion of the endoscope, so that the deployment catheter or other deployment device need not be

PCT/US2002/027450

advanced through a working channel in the endoscope. The deployment lumen 74 terminates in a distal end 78 which directs the deployment device or piercing device into tissue which has been drawn into the cavity 65. Proximally, the deployment lumen 74 may terminate in a manifold, which may additionally be provided with a flush port 128 if desired.

The central lumen 120 for receiving an endoscope extends between a distal end 122 in midsection 53 and a proximal endoscope seal 124. A distal tip 56 preferably extends beyond the midsection 53, to permit atraumatic introduction of the device. Distal tip 56 is preferably provided with a guidewire lumen 126, to facilitate over the wire placement. Guidewire lumen 126 can extend proximally throughout the length of the device, or exit at a proximal side port 127 along the side of the device such as at about the proximal end of the distal tip 56 section.

In one embodiment of the overtube illustrated in Figure 17, the tubular sheath 80 and distal end 56 assembly have an overall length on the order of about 34.8". The outside diameter of the overtube is about 0.7", and the depth of the tissue cavity between the tissue opening 58 and tissue stabilizing surface 62 is about 0.2". Any of these dimensions may be varied, to accommodate different functional characteristics and other clinical objectives of the device, as will be apparent to those of skill in the art in view of the disclosure herein.

Referring to Figure 18, there is illustrated a side elevational schematic view of a "blind" embodiment of the submucosal delivery device in accordance with the present invention. The delivery device 73 is provided with an elongate flexible body 75, having a proximal end 77 and a distal end 56. Proximal end 77 is provided with a manifold 79 which may have any of a variety of features depending upon the functionality of the device. In the illustrated embodiment, the manifold 79 is provided with a deployment device access port 81. Access port 81 is in communication with a deployment lumen 74. Deployment lumen 74 extends throughout the length of flexible body 75, and communicates with a distal end 78 at or near the tissue cavity 65 as has been discussed.

The proximal manifold 79 is further provided with a vacuum port 83. Vacuum port 83 is in communication with a vacuum lumen (not illustrated) extending

throughout the length of flexible body 75, and communicating with the tissue cavity 65 through one or more apertures 64 as has been discussed.

The embodiment of the delivery device illustrated in Figure 18 may be utilized without direct visualization. A sensor is preferably included to indicate to the clinician when sufficient tissue has been drawn into the cavity 65. Any of a variety of sensors may be devised for this purpose. In one embodiment, a pressure sensor is placed in communication with the vacuum lumen. When sufficient tissue has entered the cavity 65 to occlude the one or more vacuum ports 83, a change in pressure will be perceivable in the vacuum lumen. Any one or combination of visual, audible, or tactile feedback can be provided to a clinician, indicating that a sufficient volume of tissue has entered the cavity 65. Alternatively, any of a variety of physical pressure gages can be provided in the cavity, and utilized to detect the presence of tissue therein.

The deployment catheter 73 may be used in any of a variety of ways, and dimensions and materials may be modified to accommodate the specific intended use. For example, the deployment device 73 can be utilized to access a treatment site in the esophagus through either the nose or the mouth. Particularly in an application intended to be advanced through the nose, the distal end 56 is provided with an elongate tapered atraumatic tip to enable the device to deflect off the soft palate with minimal trauma. Distal tips for any of the Figure 16-18 or 23 versions having an axial length within the range of from about 1" to about 5" are contemplated, and may be constructed (e.g., molded) from silicone, polyurethane or other soft material.

For either nasal or oral access, the tubular body 75 may have a diameter of within the range of from about 5 mm to about 20 mm, and an axial length within the range of from about 70 cm to about 120 cm. Tubular body 75 may be constructed in any of a variety of manners well known in the catheter construction arts. For example, much of the length of tubular body 75 may comprise a two lumen extrusion with additional lumen (e.g. a guidewire lumen) being provided if additional functionalities are desired. The extrusion may comprise any of a variety of materials such as HDPE, PTFE, nylon, acrylic, PVC and other polymers which are well known in the art. The distal end 56 and distal side wall 52 including the tissue cavity 65 may be separately

formed and secured to the extrusion in any of a variety of ways, such as through heat melting, adhesive bonding and other techniques which are known in the art.

Referring to Figures 19 through 23, there are illustrated a variety of deployment devices which may be advanced through the deployment lumen 74 of any of the embodiments previously described. Referring to Figure 19, a deployment device 90 generally comprises an elongate flexible body 92 such as a deployment needle having a proximal end 94 and a distal end 96. An inner element 98 is axially movably positioned within an outer tube 100. A proximal locking mechanism 101 is provided on a proximal control 103. At the distal end 96, the outer tube 100 comprises a cavity 102 for receiving bulking media 106. A plunger 104 having a distal surface 108 is provided on the distal end of the inner element 98, and is axially movably positionable within the cavity 102. As illustrated in Figure 21, distal advancement of the inner element 98 causes the plunger 104 to distally deploy the bulking media 106.

The deployment device 90 may be constructed in any of a variety of ways which are known in the catheter construction arts. For example, either or both of the inner element 98 and outer tube 100 may be metal tubes such as hypotubes, dimensioned such that the inner element 98 is axially moveable within the outer tube 100. Alternatively, either or both of the inner element 98 and outer tube 100 may be polymeric extrusions. The inner element 98 may either be a tubular structure or a solid rod.

In an embodiment intended to advance through a deployment lumen 74 having an inside diameter of about .100", the outer tube 100 has an outside diameter of no more than about .095". In one embodiment, the inner element 98 comprises a stainless steel rod, and the outer tube 100 comprises polyimide tube. The deployment device 90 has an axial length within the range of from about 70 cm to about 100 cm, and, in the illustrated embodiment, about 100 cm.

Preferably, the length of axial travel of the inner element (e.g. push rod) 98 with respect to the outer tube 100 is sufficient to advance the distal pushing surface 108 to a position beyond the distal end 110 of the cavity 102. In an embodiment intended to deliver a hydrogel bulking device having (an unexpanded) diameter of about 2 mm and axial length of about 20 mm the deployment device 90 is constructed to permit the distal pushing surface 108 on plunger 104 to extend at least about 10 mm beyond the distal

90 89 88 87 86 85 84 83 82 81 80 79 78 77 76 75 74 73 72 71 70 69 68 67 66 65 64 63 62 61 60 59 58 57 56 55 54 53 52 51 50 49 48 47 46 45 44 43 42 41 40 39 38 37 36 35 34 33 32 31 30 29 28 27 26 25 24 23 22 21 20 19 18 17 16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1

end 110 of the cavity 102. The present inventors have determined that permitting the plunger to extend beyond the distal end of the cavity 102 permits the deployment of semi-liquid or gel form bulking agents into a submucosal tissue tract while minimizing the likelihood that trailing threads of the bulking agent will extend proximally through the tissue access pathway upon proximal retraction of the deployment device 90.

In one embodiment, the distal end 96 is provided with a sharpened point 112 for piecing a tissue surface. In this embodiment, an outer protective sheath 150 may be axially moveably carried on the outer tube 100, such that distal advancement of the outer cover 114 will shield the distal pointed tip 112. In an alternative embodiment (Figure 21), the distal end 96 is blunt.

Referring to Figure 22, there is disclosed an alternate distal end 96 for the deployment device 90, adapted to deploy an inflatable balloon 114. The balloon 114 is provided with an opening 140 on a proximal end thereof, which includes a pierceable septum or other sealable closing structure (not illustrated). A tube 142 having at least one inflation aperture 144 thereon is moveably carried within the closure structure during insertion of the deployment device 90. Proximal travel of balloon 114 along the inflation tube 142 is limited by a stop 146. Following placement within a submucosal cavity, the balloon 114 is inflated and inflation tube 142 is proximally withdrawn thereby leaving the inflated balloon in place. Deflation of the balloon is prevented by closure of the pierceable septum. The balloon may be deployed by advancing the delivery system into the submucosal space, retracting covering sheath 147 to expose the balloon 114, inflating the balloon 114 through inflation tube 142 and withdrawing the catheter system leaving the balloon in place.

Referring to Figure 23, there is illustrated a schematic view of a reflux repair system in accordance with the present invention. As has been previously described, a push rod 98 is utilized to distally advance a prosthesis 106 out of the distal end 96 of a tubular deployment device such as a deployment needle or a sheath 150. In the illustrated system, a dilating trocar assembly of needle 90 and dilator 152 is axially movably carried within a sheath 150. The dilating trocar and sheath assembly is axially moveably advanced through the overtube sheath 80 to the cavity 65 as has been discussed. In one embodiment, the needle 90 has an outside diameter of about 0.030 in.

and a length extending out of the dilator of about 0.10 in. The dilator 152 comprises polyethylene or other polymers or materials known in the art and has a tapered outside diameter from about 0.080 in. at its proximal end to about 0.030 in. at its distal end. The dilator 152 has an axial length of about 85 cm, and a central lumen for receiving the
5 needle 90. The dilator may be secured to the needle in any of a variety of ways such as with known biocompatible adhesives or mechanical interference.

In the illustrated embodiment, an overtube handle or manifold 79 is provided with a sheath seal 154 and a scope seal 156 for sealingly receiving the delivery sheath and the endoscope as has been discussed.

10 The dilating trocar and sheath assembly allows the delivery of a prosthesis having a greater cross-sectional dimension than the initial puncture. For example, the needle 90 may be dimensioned to provide a 0.5 mm hole in the tissue, and then be used to introduce a volume of fluid submucosally to create a cavity, as is discussed elsewhere herein. The needle, dilator and sheath are then advanced into the cavity, providing a 2
15 to 3 mm channel into the submucosal plane. The dilator 152 and needle 90 assembly may thereafter be proximally withdrawn, so that the prosthesis 106 may be deployed through the sheath 150 into the preformed cavity. Following deployment of the prosthesis 106, the sheath 150 is proximally retracted from the tissue. Upon removal of the sheath 150, the tissue surrounding the tissue tract constricts back to a smaller cross
20 section, thereby providing resistance to proximal migration of the deployed prosthesis 106.

25 In one application of the method of the present invention, the reflux repair system is positioned within the esophagus and tissue is drawn into the cavity 65 as has been discussed. A blebbing needle, generally within the range of from about 20 to about 25 gauge, and, in one embodiment, 23 gauge, is introduced into the tissue to create a cavity. Approximately 0.5 to about 5 cc of fluid, such as saline is introduced into the tissue. The blebbing fluid may additionally comprise any of a variety of additives such as antimicrobial compounds, contrast agents for visualization, antibiotics, lidocaine, epinephrine, hyaluronic acid, PEG, colorants or others as may desired. In an
30 embodiment in which the blebbing needle is distinct from the dilating trocar assembly,

RECEIVED
U.S. PATENT AND TRADEMARK OFFICE

the blebbing needle is thereafter retracted proximally from the site, and withdrawn from the overtube sheath 80.

A dilating trocar sheath assembly is thereafter advanced distally through the tissue tract, thereby increasing the diameter of the tissue tract from approximately equal to the blebbing needle, to a sufficient diameter to receive the sheath 150. Sheath 150 has an outside diameter within the range of from about 0.085 in. to about 0.095 in., and, in one embodiment, about 0.090 in. Once the sheath 150 is in position through the tissue tract and into the tissue cavity, the trocar tip 96 and dilator 152 assembly is proximally retracted to leave the sheath 150 in position to provide access to the tissue cavity. The prosthesis 106 is thereafter advanced through the sheath 150 and into the tissue cavity using the push rod 98.

The prosthesis 106 may be advanced using the push rod 98 directly through the sheath 150. Alternatively, a prosthesis delivery assembly may be provided, in which the prosthesis 106 is positioned within the distal end of a tubular delivery needle or cannula as has been discussed in connection with previous embodiments. This needle preferably has an inside diameter of at least about 1 mm, and, in one embodiment, about 2 mm, to retain an expandable prosthesis 106 therein. The delivery cannula carrying the prosthesis 106 and push rod 98 may be advanced through the sheath 150 and into the cavity. The distal end of the delivery needle is preferably positioned at the distal end of the cavity, and the delivery needle is proximally retracted while the push rod 98 is maintained in its axial position, thereby deploying the prosthesis 106 into the distal portion of the cavity. The delivery needle and push rod 98 may thereafter be retracted from the cavity, and the vacuum released to disengage the overtube sheath from the tissue surface. In an alternate application of the method, the prosthesis is carried in and deployed directly from the needle, and the sheath may be omitted.

Prior to disengaging the overtube sheath 80 from the tissue wall, the tissue tract may be sealed or plugged to further reduce the likelihood of migration of the prosthesis 106 from the cavity. This may be particularly desirable in an embodiment in which the prosthesis 106 is delivered in the form of a cure in place liquid or gel. The tissue tract may be plugged in any of a variety of ways, such as by injecting a collagen, wax or

other plug. Alternatively, the tissue tract may be sutured or clipped, or sealed or filled with an adhesive with or without a patch.

As with previous embodiments of the method and devices, the prosthesis 106 deployed using the system illustrated in Figure 23 may also be explanted. Removal of the prosthesis 106 may be accomplished by identifying the location of the prosthesis 106, establishing a tunnel or access pathway through the tissue to the prosthesis 106, and applying suction to draw the prosthesis 106 out from beneath the tissue and into the distal end of a removal device such as an endoscope with a cylindrical extension or cap to allow the application of a suction to a portion of the tissue surface. The tunnel may be established either by the distal advancement of a needle or other cutting tool (e.g. mechanical cutter, laser, RF electrode) or by merely applying suction in the vicinity of the original tissue tract. The hydrogel prostheses disclosed herein are particularly suited for removal, since they do not tend to experience tissue ingrowth.

Removal of the hydrogel or other implant can also be accomplished using mechanical explantation devices, such as any of a variety of biopsy tools or mechanical graspers. Removal can also be accomplished by applying pressure on tissue above a first end of the implant to cause the implant to advance in a second direction, *i.e.*, by pressing the implant out. Depending upon the composition of the implant, it may also be dissolved or degraded in place, such as by the introduction of a solvent or initiator.

The deployment or delivery systems disclosed in Figure 19 through 23, among other deployment devices, can be used in accordance with the present invention to deliver any of a wide variety of expandable bulking devices or other submucosal prostheses. Suitable bulking devices fall into either of two broad categories. The first are bulking devices which inherently expand to achieve a predetermined configuration. This category includes a wide variety of capsules, foams and hydrogels as have been disclosed previously herein. The second category includes fluids or gels which do not inherently assume any particular shape upon expansion or solidification, but which are able to achieve a predetermined shape *in situ* when used in accordance with the present invention.

Concerning the first category, a variety of capsules and foams have already been disclosed herein. In addition, a variety of hydrogels may be used such as those

disclosed in U.S. Patent No. 4,943,618 issued July 24, 1990 to Stoy et al., entitled Method for Preparing Polyacrylonitrile Copolymers by Heterogeneous Reaction of Polyacrylonitril Aquagel, and U.S. Patent No. 5,252,692 issued October 12, 1993 to Lovy et al. entitled Hydrophilic Acrylic Copolymers and Method of Preparation, the disclosures of both of which are incorporated in their entireties herein by reference. Preferably, a hydrogel or other material will be selected which has an expansion ratio on the order of at least about 100% and preferably in excess of 500%, particularly in the transverse direction. Thus, a hydrogel rod having a diameter of about 1 mm when positioned within the cavity 102 will preferably expand to a cross section of about 5 or 6 millimeters or greater *in situ*. Preferably, the hydrogel or other bulking media will exhibit a sufficient expansion rate that it will expand sufficiently to lock in place before migrating from the deployment site such as through the introduction tissue tract.

Another aspect of the present invention is the ability to introduce a bulking media in a fluid or gel form which possesses no inherent ability to achieve a predetermined shape, yet, when used with the devices of the present invention, will produce a bulking structure having a predetermined configuration. This is achieved through the interaction between the devices disclosed herein and the anatomy of the esophagus.

The central esophageal lumen is surrounded by a mucosa layer having a thickness on the order of from about 1.0 to about 2.0 mm. Below the mucosa is the submucosa, having a thickness on the order of about 0.5 to about 1 mm. Below the submucosa is a muscle layer having a variable thickness, generally on the order of about 2 mm to about 3 mm. When mucosa is drawn into the cavity on the delivery device of the present invention, a reproducible low pressure region is created in the submucosa which corresponds in shape to the shape of the mucosa which has been drawn into the cavity. The delivery channel directs a deployment needle or other device through the mucosa and directly into the low pressure region of the submucosa. Thus, in accordance with the present invention, a polymerizable or otherwise hardenable fluid or gel may be injected into the low pressure zone in the submucosa at the target site, and that fluid or gel will assume a shape which is strongly influenced by the shape of the opening 58 and depth of the cavity 65. In addition, the muscle layer is substantially

unaffected by the application of vacuum to the mucosa using the devices disclosed herein, because the deployment lumen directs the deployment device generally in parallel to the muscle layer. This minimizes the risk of piercing the muscle layer beneath the submucosa. Among other complications from piercing the muscle layer, the
5 aorta and vagus nerve are positioned closely outside of that layer.

Any of a variety of fluids or gels may be utilized, such as UV curable materials, heat or catalytically initiated polymerizable materials, and others which can be optimized through routine experimentation by those of ordinary skill in the art in view of the disclosure herein. Another useful class of bulking media includes biocompatible
10 polymers which are soluble in a biocompatible solvent but insoluble in the submucosal tissue. The biocompatible solvent is soluble or dispersible in the tissue, such that the biocompatible solvent diffuses away from the biocompatible polymer *in situ*, thereby permitting the biocompatible polymer to precipitate, polymerize, or otherwise harden into a bulking mass. In one embodiment, the bulking media further includes a contrast
15 agent, to permit visualization of the bulking mass during and following implantation of the bulking media. Examples of suitable bulking media are disclosed in U.S. Patent No. 5,785,642, issued July 28, 1998 to Wallace et al., entitled Methods for Treating Urinary Incontinence in Mammals, the disclosure of which is incorporated in its entirety herein by reference.

20 Although the foregoing invention has been disclosed in terms of certain preferred embodiments, other specific embodiments can be constructed in view of the disclosure herein without departing from the spirit of the scope of the present invention. Accordingly, the scope of the Applicant's invention is to be determined by reference to the attached claims, which are not limited to any of the particular embodiments
25 disclosed herein.

WHAT IS CLAIMED IS:

1. A method of implanting a bulking device beneath the mucosa in the lower esophagus, comprising the steps of:

puncturing the mucosa with a device having a first cross sectional area;

creating a pocket beneath the mucosa and in communication with the puncture;

enlarging the puncture; and

introducing a bulking device through the puncture and into the pocket.

2. A method of implanting a bulking device as in Claim 1, wherein the introducing step comprises introducing an expandable bulking device.

3. A method of implanting a bulking device as in Claim 2, wherein the bulking device is expandable from an introduction cross sectional area to an enlarged cross sectional area, and the introduction cross sectional area is greater than the first cross sectional area.

4. A method of implanting a bulking device as in Claim 1, wherein the introducing step comprises introducing a hydrogel bulking device.

5. A method of implanting a bulking device as in Claim 1, wherein the creating a pocket step comprises introducing a volume of fluid beneath the mucosa.

6. A method of implanting a bulking device as in Claim 5, wherein the creating a pocket step comprises introducing within the range of from about 0.5 cc to about 5 cc of fluid beneath the mucosa.

7. A method of implanting a bulking device as in Claim 5, wherein the fluid comprises saline.

8. A method of implanting a bulking device as in Claim 5, wherein the fluid comprises an additive selected from the group consisting of hyaluronic acid, lidocaine, epinephrine, antibiotics, polyethylene glycol, colorants, and contrast media.

9. A method of implanting a bulking device as in Claim 5, wherein the introducing a volume of fluid is accomplished using an injection needle.

10. A method of implanting a bulking device as in Claim 9, wherein the needle is within the range of from about 18 gauge to about 30 gauge.

11. A method of implanting a bulking device as in Claim 1, wherein the enlarging step comprises introducing a dilator through the puncture.

12. A method of implanting a bulking device as in Claim 11, wherein the dilator removably carries an introducer sheath.

5 13. A method of implanting a bulking device as in Claim 12, further comprising the steps of removing the dilator from the introducer sheath and introducing the bulking device through the introducer sheath and into the pocket.

14. A method of treating a condition in the lower esophagus, comprising the steps of:

10 creating a pocket beneath the mucosa in the lower esophagus; and positioning an expandable bulking device within the pocket.

15. A method as in Claim 14, wherein the bulking device comprises a hydrogel.

16. A method as in Claim 14, wherein the bulking device is expandable in response to exposure to fluid.

17. A method as in Claim 15, wherein the bulking device has a diameter prior to implantation within the range of from about 0.2 mm to about 5 mm.

18. A method as in Claim 17, wherein the bulking device has a cross section prior to implantation of no more than about 2.5 mm.

20 19. A method as in Claim 14, further comprising the step of removing the bulking device from the pocket.

20. A method as in Claim 19, wherein the removing step is accomplished by creating a passageway through tissue to the bulking device.

21. A method as in Claim 20, wherein the removing step further comprises using suction.

22. A method as in Claim 19, wherein the removing step comprises introducing a solvent to dissolve the bulking device.

23. A method as in Claim 22, wherein the solvent comprises DMSO.

24. A method as in Claim 19, wherein the removing step is accomplished 30 utilizing a laser.

25. A method as in Claim 19, wherein the removing step is accomplished using an energy source.

26. A method as in Claim 19, wherein the removing step comprises cutting the bulking device into pieces.

5 27. A method of explanting a bulking device positioned beneath the mucosa in the vicinity of the lower esophageal sphincter, comprising the steps of:

locating a bulking device positioned beneath the esophageal mucosa;
establishing a passage through the mucosa; and
explanting the bulking device through the passage.

10 28. A method of explanting a bulking device as in Claim 27, wherein the explanting step is accomplished using an endoscope.

29. A method of explanting a bulking device as in Claim 27, wherein the establishing a passageway step is accomplished using an RF electrode.

15 30. A method of explanting a bulking device as in Claim 27, wherein the establishing a passageway step is accomplished using a sharpened instrument.

31. A method of explanting a bulking device as in Claim 27, wherein the explanting step is accomplished by applying suction.

32. A method of explanting a bulking device as in Claim 27, wherein the explanting step comprises pushing the bulking device through the passage.

20 33. A method of explanting a bulking device as in Claim 27, wherein the explanting step is accomplished using a mechanical explanting tool.

34. A method of implanting a bulking device beneath the mucosa in the lower esophagus, comprising the steps of:

puncturing the mucosa with a device having a first cross sectional area;
enlarging the puncture; and
introducing an expandable bulking device through the puncture to a position beneath the mucosa.

35. A method of implanting a bulking device as in Claim 34 wherein the introducing step comprises introducing a hydrogel bulking device.

30 36. A method of implanting a bulking device as in Claim 34, wherein the enlarging step comprises advancing a dilator through the puncture.

37. A method of implanting a bulking device as in Claim 36, further comprising the steps of advancing a tube through the enlarged puncture and introducing the bulking device through the tube.

**METHOD AND DEVICE FOR TREATING GASTROESOPHAGEAL
REFLUX DISEASE**

ABSTRACT OF THE DISCLOSURE

5 Disclosed is a delivery device for controllably delivering a prosthetic bulking device below a tissue surface such as below the mucosa to treat gastroesophageal reflux disease. The delivery device may be embodied in a deployment catheter, an endoscope, or an endoscope attachment. The bulking device may additionally be explanted from beneath the mucosa. In one embodiment, the bulking device comprises a hydrogel.

10

15

H:\DOCS\GVH\GVH-2391.DOC/jt2
092200
H:\DOCS\GVH\GVH-2742.DOC
102500

09/762,002 "A10/30000

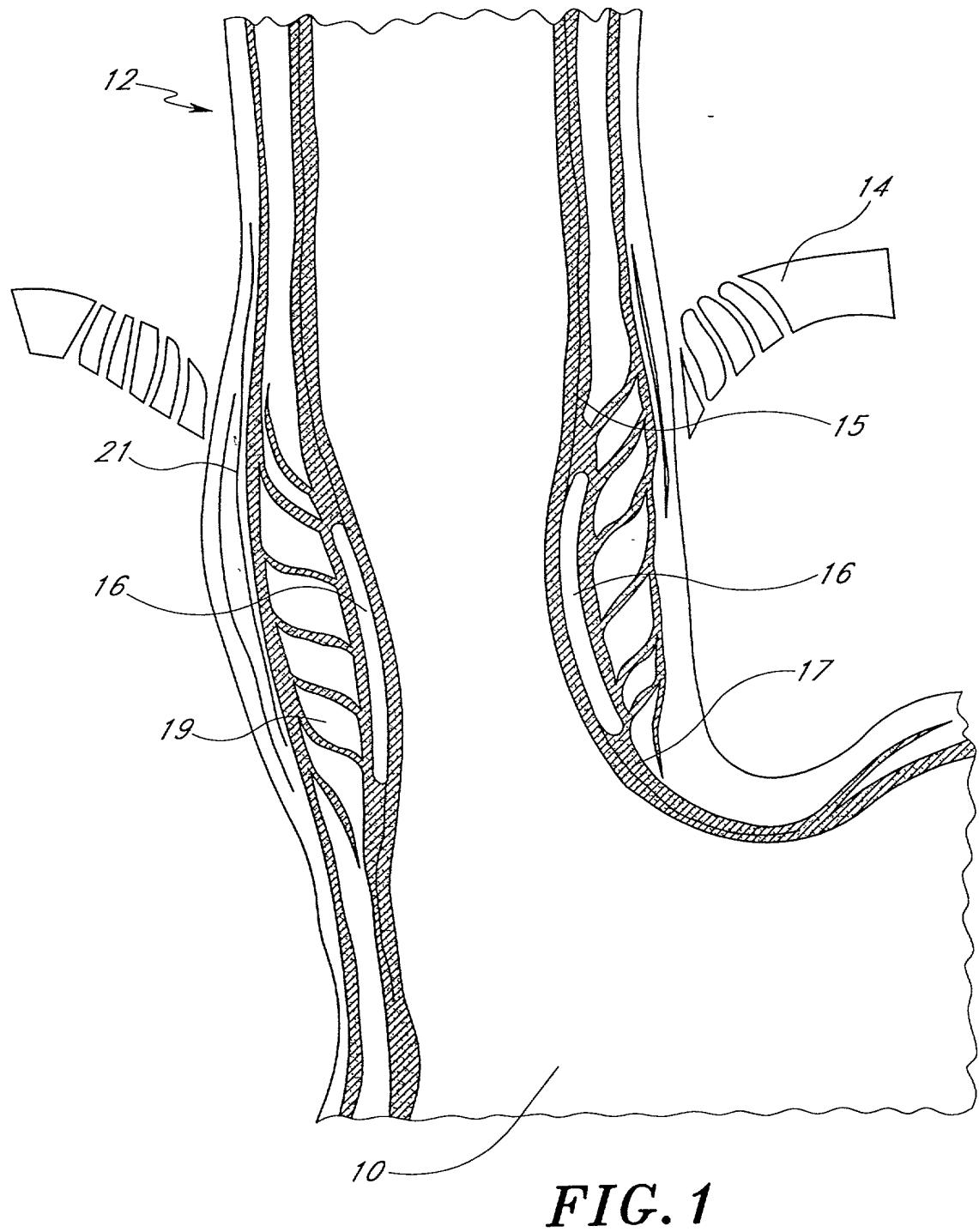


FIG. 1

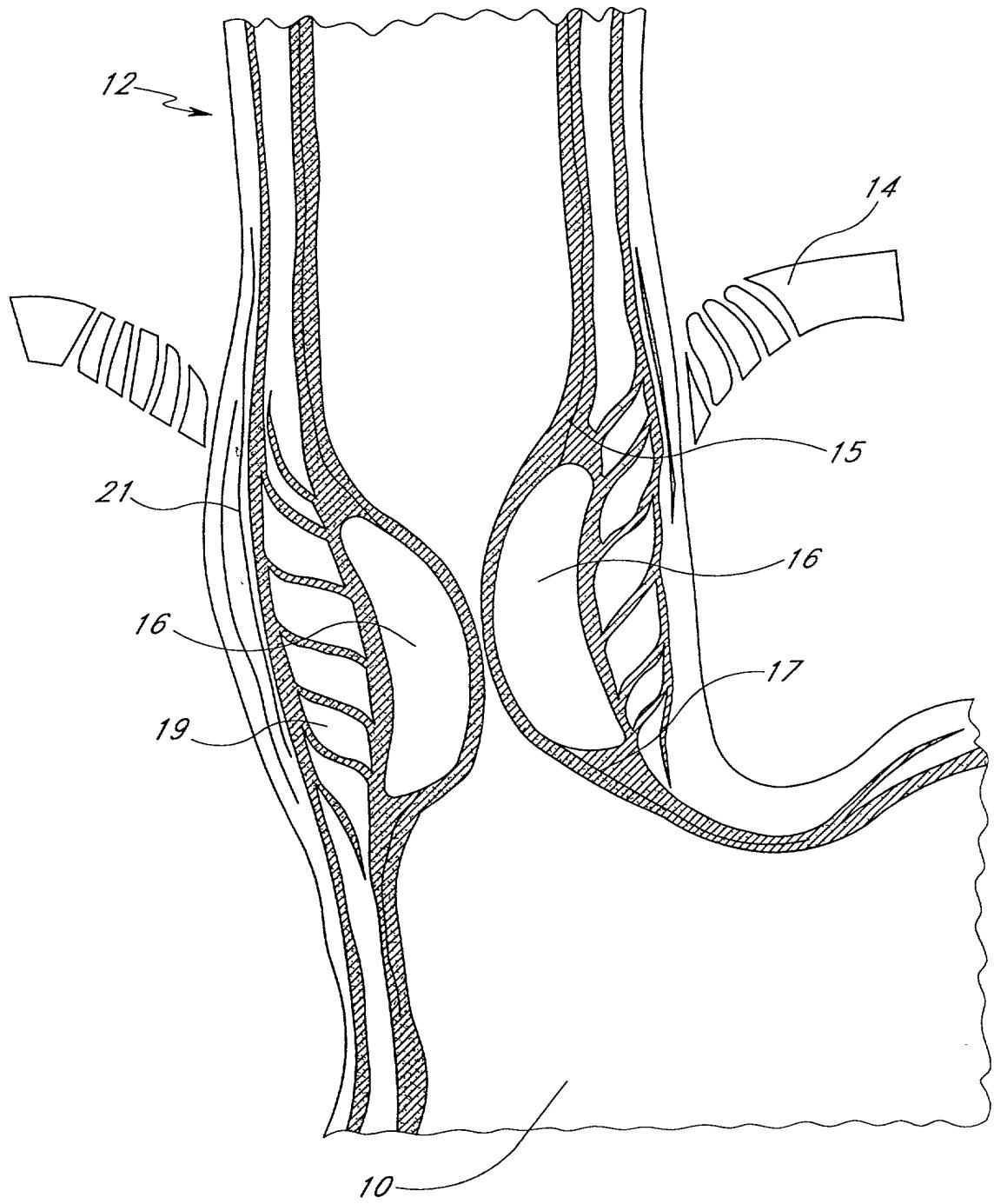


FIG. 2

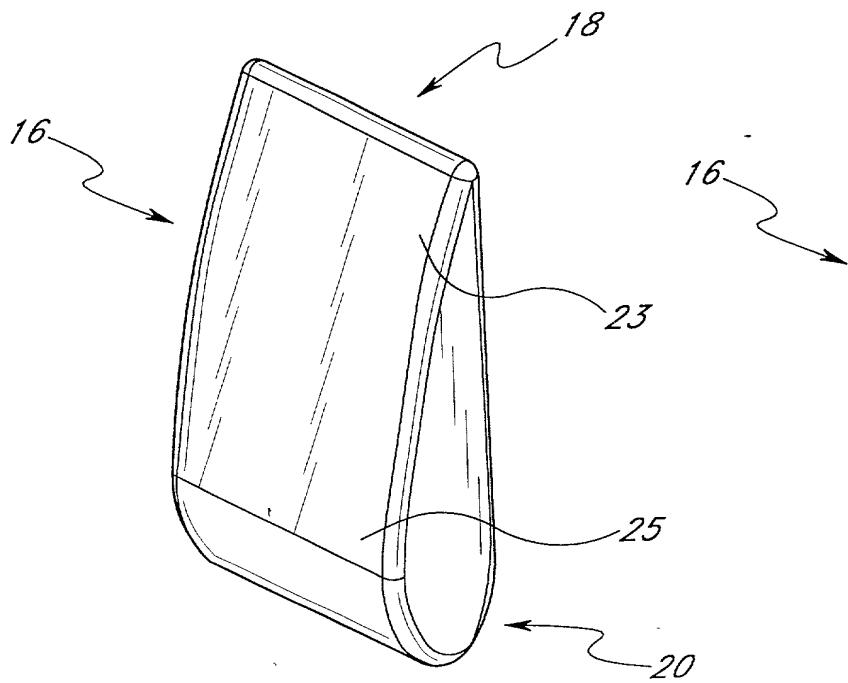


FIG. 4

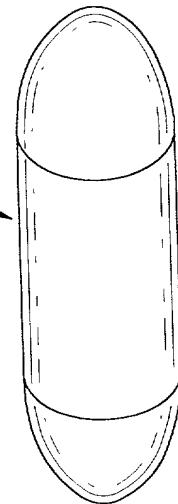


FIG. 3

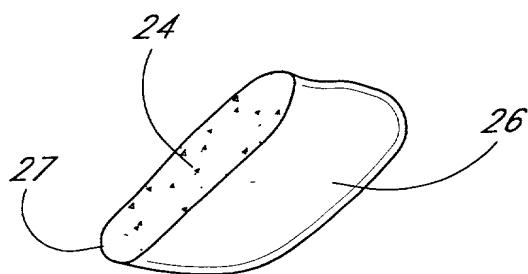


FIG. 5

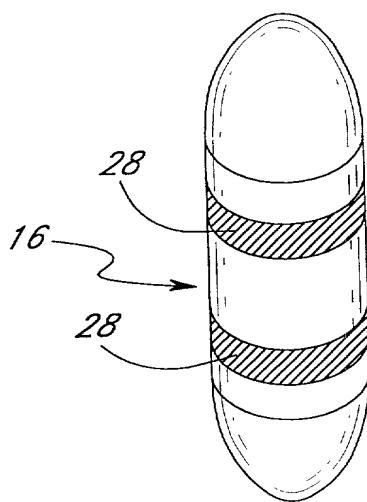


FIG. 6

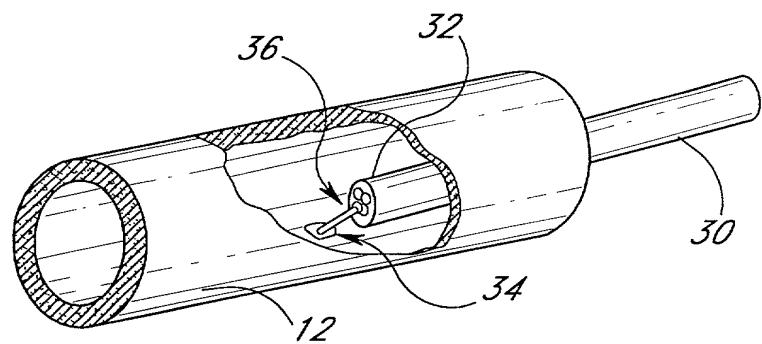


FIG. 7

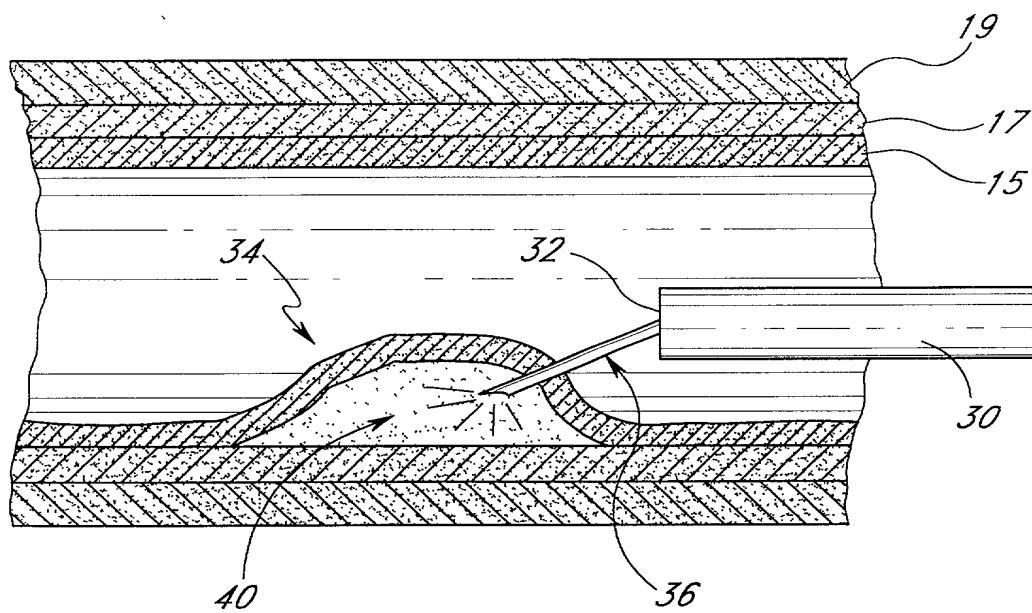


FIG. 8

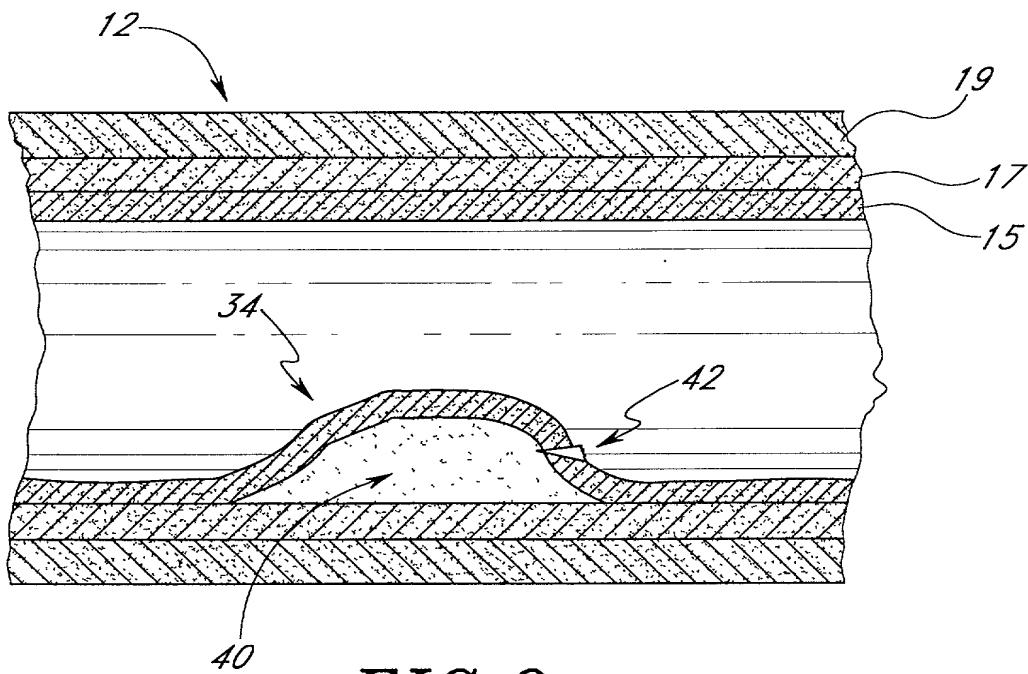


FIG. 9

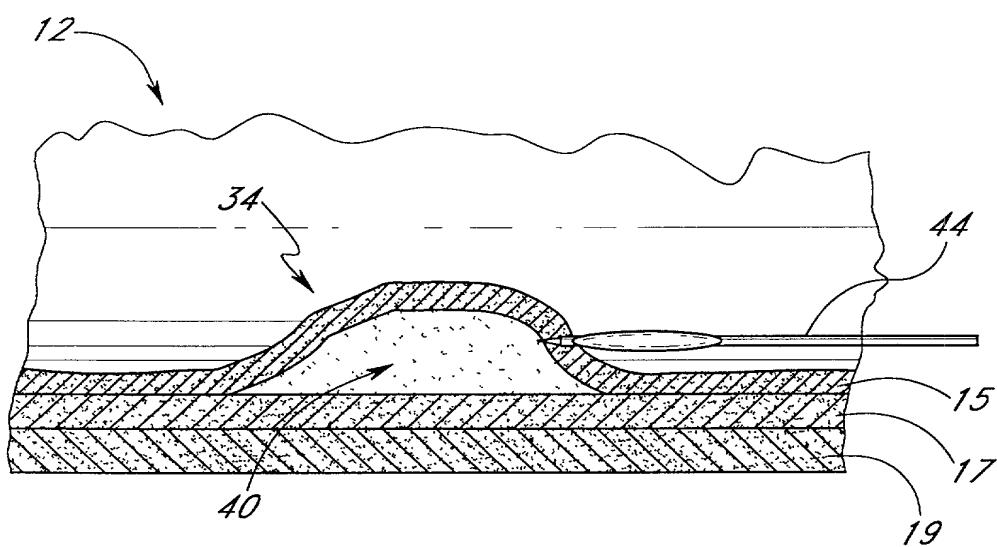


FIG. 10

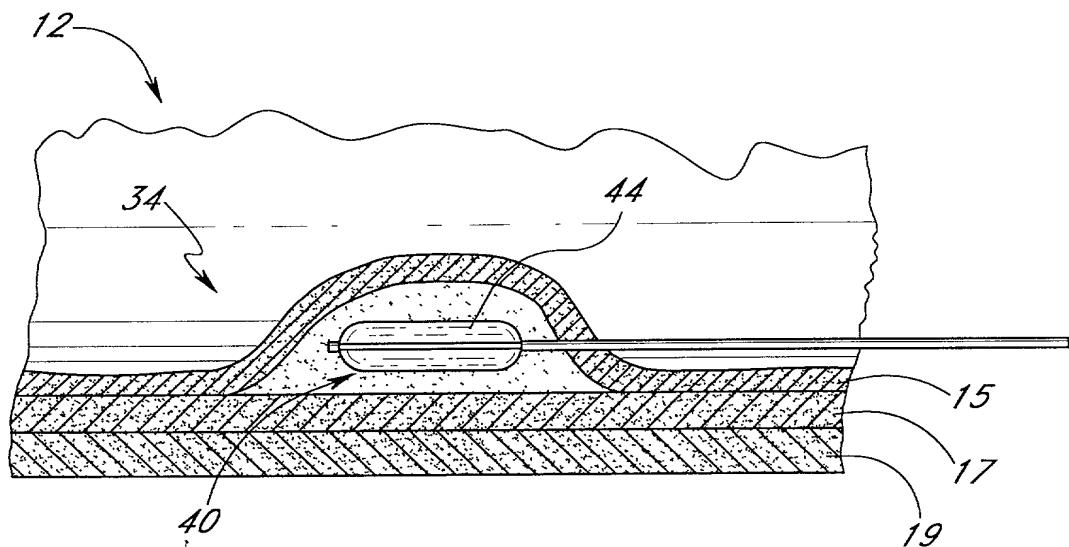


FIG. 11

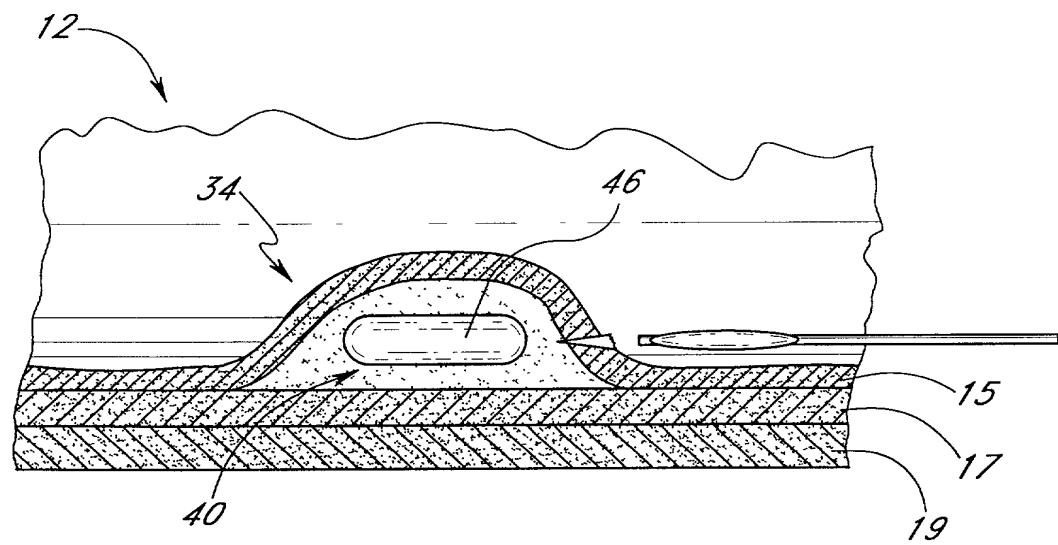


FIG. 12

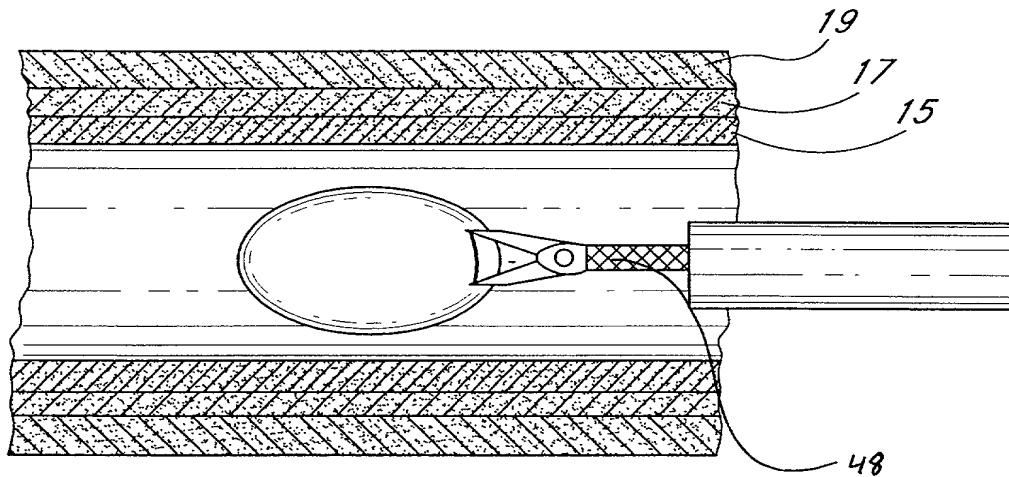


FIG. 13

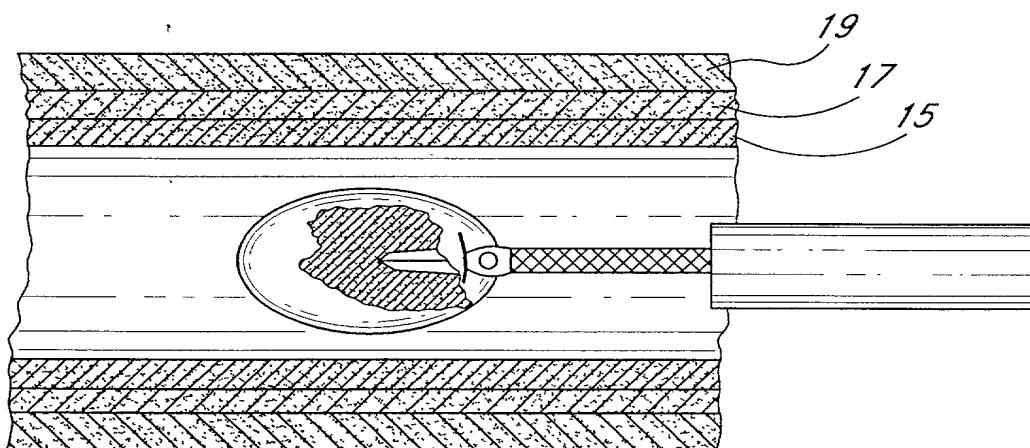


FIG. 14

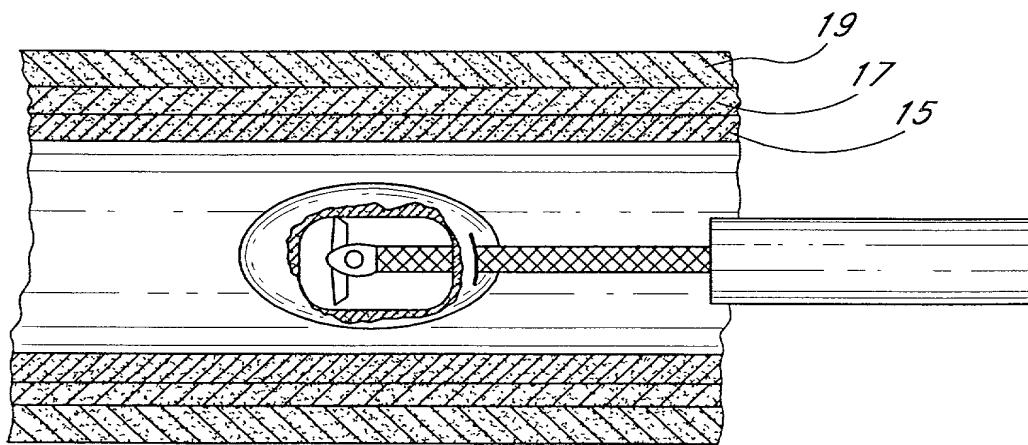


FIG. 15

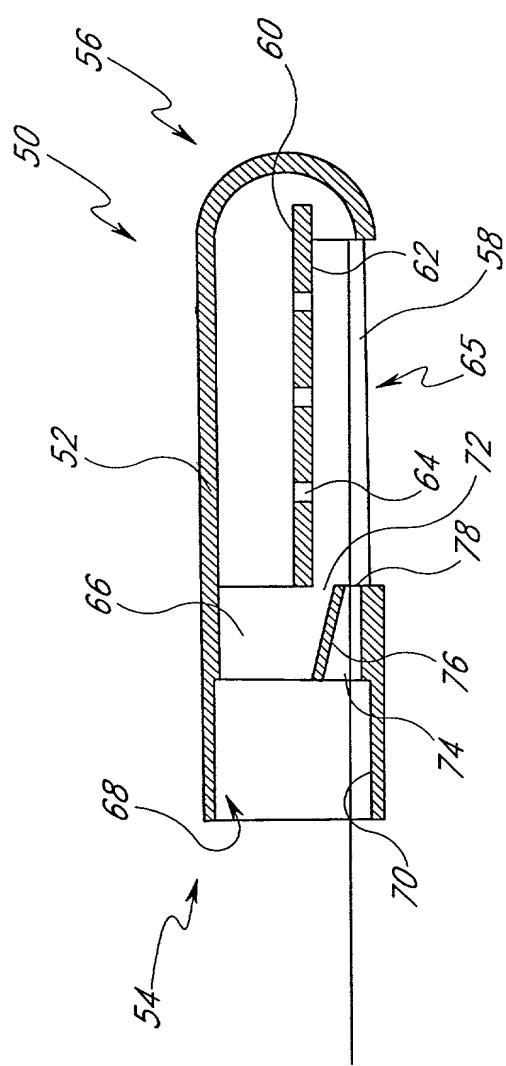


FIG. 16

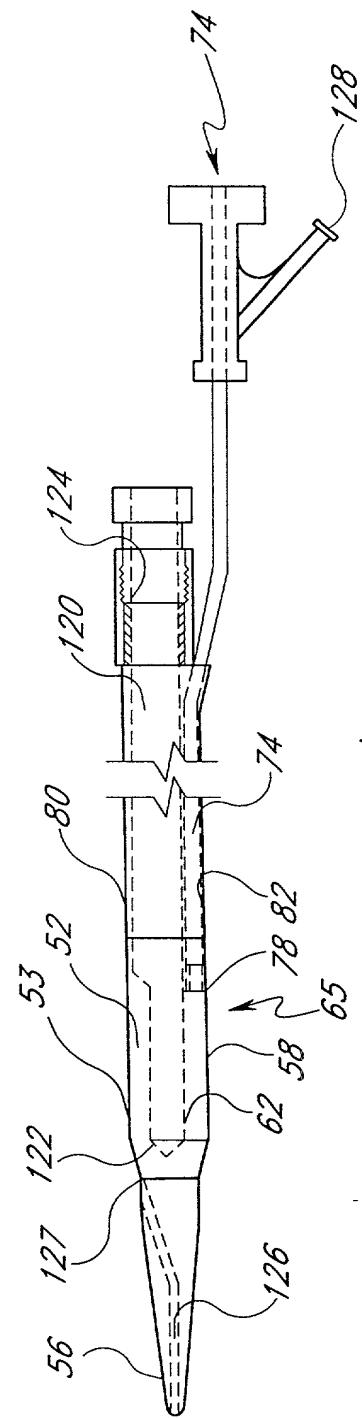


FIG. 17

100301 20020460

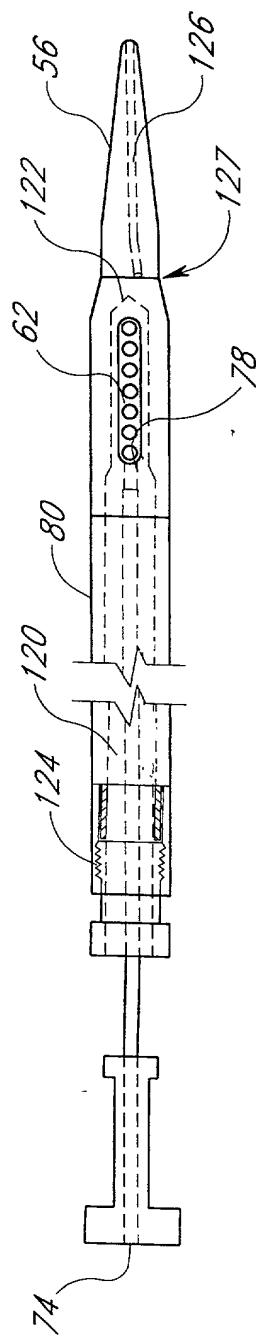


FIG. 17A

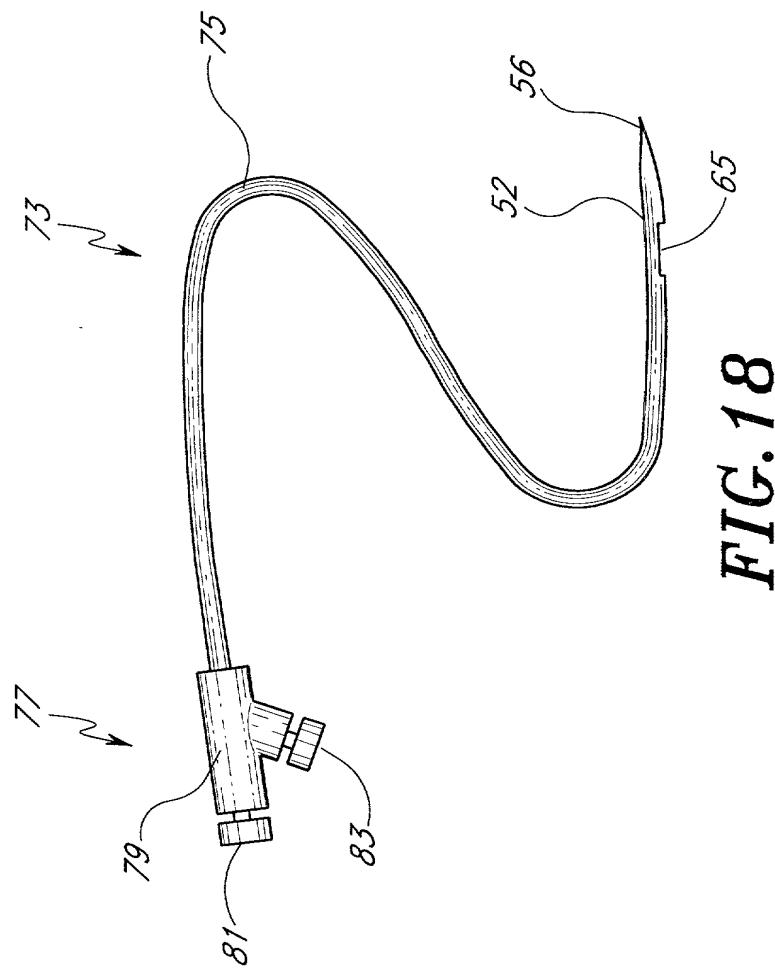


FIG. 18

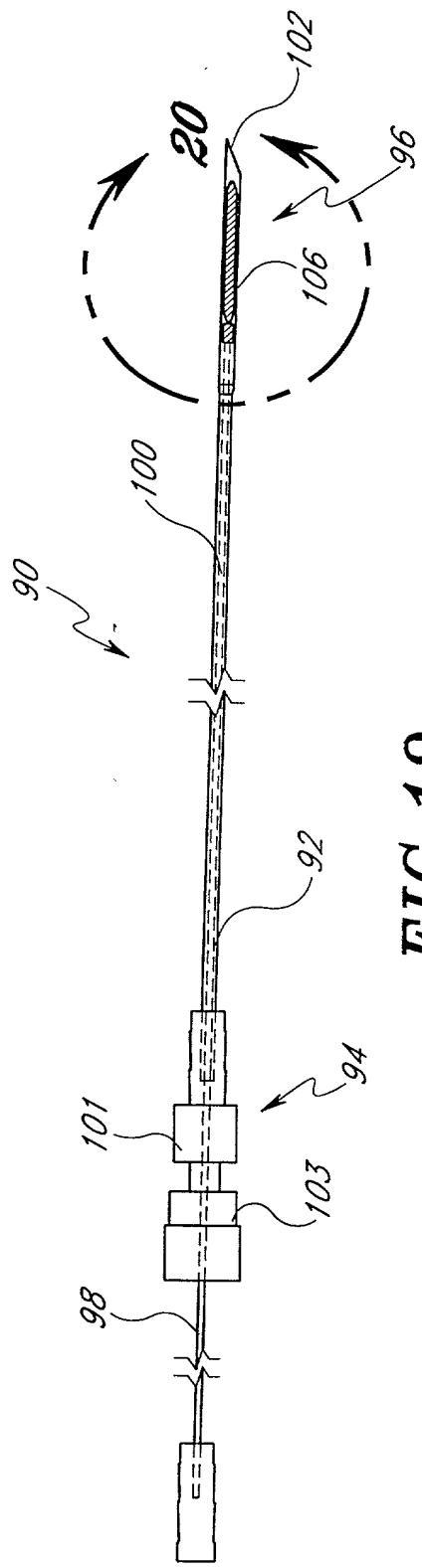


FIG. 19

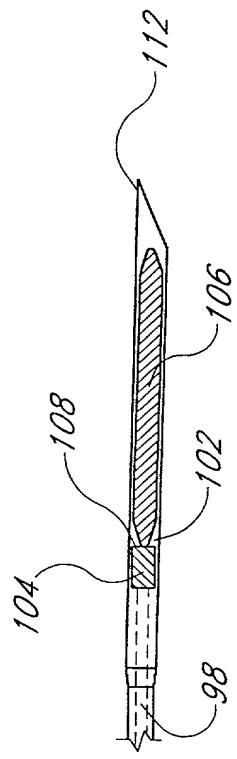


FIG. 20

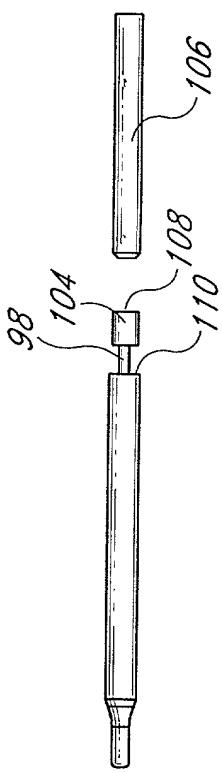


FIG. 21

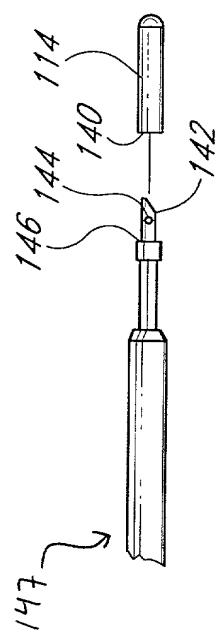


FIG. 22

FIG 23

